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Diagnostic value and prognostic implications of early cardiac magnetic resonance in survivors of out of hospital cardiac arrest

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ABSTRACT

Background: In patients who survived out-of-hospital cardiac arrest (OHCA) it is crucial to establish the underlying cause and its potential reversibility. **Objective:** We assessed the incremental diagnostic and prognostic role of early cardiac magnetic resonance (CMR) in survivors of OHCA. **Methods:** Among 139 consecutive OHCA patients, we enrolled 44 (median age 43 years; 84% males) patients who underwent coronary angiography and CMR ≤7 days after admission. The CMR protocol included T2-weighted sequences for myocardial edema and late gadolinium-enhancement (LGE) sequences for myocardial fibrosis. **Results:** Coronary angiography identified obstructive coronary artery disease (CAD) in 18/44 patients, in whom CMR confirmed the diagnosis of ischemic heart disease by demonstrating subendocardial or transmural LGE; the presence of myocardial edema allowed to differentiate between acute myocardial ischemia (N=12) and post-infarction myocardial scar (N=6). Among the remaining 26 patients without obstructive CAD, 19 (73%) showed at CMR dilated cardiomyopathy (N=5), myocarditis (N=4), mitral valve prolapse associated with LGE (N=3), ischemic scar (N=2), idiopathic non-ischemic scar (N=2), arrhythmogenic cardiomyopathy (N=1), hypertrophic cardiomyopathy (N=1) and Tako-Tsubo cardiomyopathy (N=1). In this subgroup, 6/26 (23%) had myocardial edema. During a mean follow-up of 36±17 months, all 18 patients with myocardial edema had an uneventful outcome while 9/26 (35%) without myocardial edema experienced sudden arrhythmic death (N=1), appropriate defibrillator interventions (N=5) and non-arrhythmic death (N=3) (p=0.006). **Conclusions:** In survivors of OHCA, early CMR with a comprehensive tissue characterization protocol provided additional diagnostic and prognostic value. The identification of myocardial edema was associated with a favorable long-term outcome.

Key Words: cardiac arrest; cardiopulmonary resuscitation; cardiac blunt trauma; cardiac magnetic resonance; implantable cardioverter defibrillator; secondary prevention; ventricular arrhythmia.

INTRODUCTION

Out-of-hospital cardiac arrest (OHCA) due to ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) can be caused by ischemic and non-ischemic heart diseases. In patients who suffered OHCA, clinical investigations aim at establishing what is the underlying disease and whether the cause of the arrhythmia is reversible. This is particularly relevant for decision to implant a defibrillator (ICD), that is not indicated in patients who experienced VT/VF due to a reversible myocardial injury like that secondary to myocardial ischemia of acute coronary syndromes or myocarditis[1-2]. In this contest, the interpretation of standard investigations such as ECG, echocardiography and coronary angiography may not be straightforward and nonspecific findings secondary to the cardiac arrest and subsequent resuscitation may act as confounders[3-5].

Cardiac magnetic resonance (CMR), in addition to accurate assessment of ventricular function, allows the identification of myocardial tissue changes such as myocardial edema as evidenced by increased signal intensity on T2-weighted sequences and myocardial fibrosis by late gadolinium enhancement (LGE) on post-contrast sequences[6]. In the evaluation of patients who survived OHCA, the combination of sequences for myocardial edema and fibrosis has the potential to distinguish an acute and potentially reversible injury from a chronic and irreversible lesion[7].

The aim of the present study was to prospectively evaluate the incremental diagnostic and prognostic value of early (within one week after admission) CMR, enhanced with an accurate tissue characterization protocol including sequences for myocardial edema and fibrosis, in OHCA survivors.

METHODS

The study included all survivors of arrhythmic OHCA who were admitted to our institution during the study period 2011-2016 and underwent coronary angiography and CMR within one week of hospitalization. The CMR was performed in all patients who could be weaned from mechanical ventilation, had no neurological impairment and had no contraindications to CMR. The study complies with the Declaration of Helsinki, was approved by the Ethical Committee and all patients agreed to participate.

Coronary angiography

Coronary angiography was performed in all patients: at admission in those with ST-segment elevation at post-resuscitation ECG or in those with high clinical suspicious of ongoing myocardial ischemia; delayed in the others. A culprit coronary lesion was defined as obstructive (≥70%) CAD with TIMI 0/1 flow with abrupt closure, or TIMI 2/3 flow with features suggestive of thrombus or ulcerated plaques, ST segment and T wave changes in the corresponding ECG location, and evidence of matching regional wall motion abnormality on left ventriculogram or echocardiogram[8].

Contrast-enhanced cardiac magnetic resonance

The CMR scan protocol systematically included steady-state free precession sequence (true FISP) cine images for morpho-functional evaluation, T2-weighted sequences for detection of myocardial edema and post-contrast sequences for detection of LGE. Details are reported in the supplemental file.

Follow-up

Patients were followed-up with serial outpatient evaluations or with telephonic interviews to determine the alive status and whether they reached the composite arrhythmic end-point including sudden death, cardiac arrest due to VF, sustained VT and appropriate ICD intervention. Sudden

death was defined as any natural death occurring instantaneously or within 60 minutes from symptoms onset. Appropriate ICD intervention was defined as an ICD shock delivered in response to a ventricular tachyarrhythmia >170 bpm and documented by stored intracardiac ECG data. All ICD interventions were adjudicated as appropriate or inappropriate by two electrophysiologists (AZ, DC) based on morphologic features, tachycardia onset, rate stability and atrial electrograms (when available). ICD were programmed according to the MADIT-RIT trial high-rate or delayed-therapy programming[9].

Statistical Analysis

Continuous and categorical variables are expressed as median (with 25^{th}-75^{th} %iles), and n (%), respectively. Because of the small sample size, normality distribution was not assumed. Categorical variables were compared by using the chi-square or Fisher exact test, as appropriate. Continuous data were compared using the Mann-Whitney U test. A p-value of <0.05 was considered statistically significant. Data were analysed with SPSS® version 23 (IBM®).

RESULTS

Among a consecutive series of 139 patients admitted for OHCA**,** 37 (27%) died during the acute phase. Among the remaining 102 patients, 58 (42%) were not recruited because of neurological impairment and/or mechanical ventilation (N=52), the presence of a no-MRI compatible pacemaker (N=4) or poor CMR quality images (N=2). Forty-four patients [median age 43 years (39-62 years); 84% males] met the enrollment criteria and constituted the definitive study cohort. (Table 1). Coronary angiography was performed at admission in 20 (45%) patients, including 7 (16%) with post-resuscitation ST-segment elevation, and within 4 days in the remaining patients.

Obstructive CAD

Angiographic evidence of obstructive coronary disease (≥1 coronary stenosis ≥70%) was found in 18 (41%) patients. A clear culprit coronary lesion was identified in 10 patients, 5/5 with single vessel disease and 5/13 with multiple vessels disease.

Cardiac magnetic resonance findings are summarized in Table 2.

The presence of myocardial edema at T2-weighted sequences consistent with an acute ischemic injury in 12/18 (67%) patients (Figure 1). In all cases, the regional distribution of myocardial edema was concordant with the territory which was tributary of a coronary artery with obstructive stenosis or occlusion. In 10 patients with an identifiable culprit coronary lesion, the regions of myocardial edema were always concordant with the regional distribution of the culprit coronary artery. Myocardial edema was present in 2 of the 8 patients with multiple vessels disease and no identifiable culprit coronary lesion. The Peak troponin I (normal value <0.017 ug/L) was significantly higher in patients with [12.2 ug/L (2.1-104.8)] compared with those without [2.8 ug/L (1.2-26.1)] LV myocardial edema ($p = 0.02$).

Left ventricular LGE with a subendocardial or transmural distribution was demonstrated in all patients (Figure 2). Among the 12 patients with myocardial edema, the regional distribution of LV

LGE corresponded to the edematous LV segments in 8 (consistent with an acute myocardial ischemic injury without previous myocardial infarction) and extended to other non-edematous segments in 4 (consistent with an acute myocardial ischemic injury superimposed on a previous post-myocardial infarction scar).

Right ventricular LGE was present in a patient with right ventricular myocardial infarction due to occlusion of the proximal right coronary artery.

No obstructive CAD

Among the 26 (59%) patients with non-obstructive CAD, coronary angiography revealed normal coronary arteries in 20 and non-obstructive coronary artery stenosis in 6. A negative history of cardiac disease at risk of sudden cardiac death was documented in all but one patient with a previous diagnosis of HCM. CMR allowed to identify a pathological myocardial substrate in 19 (73%) consistent with dilated cardiomyopathy (N=5); acute myocarditis (N=4, Figure 3), mitral valve prolapse associated with LGE (N=3, Figure 4); ischemic heart disease (N=2), isolated non-ischemic left ventricular scar (N=2, Figure 5), arrhythmogenic cardiomyopathy (N=1), hypertrophic cardiomyopathy (N=1) and Tako-Tsubo cardiomyopathy (N=1) (Table 2).

Left ventricular myocardial edema was present in 6 (23%) patients. The following regional distribution patterns of myocardial edema were identified: 1) midmyocardial or subepicardial pattern involving the infero-lateral LV wall in 4 patients, consistent with a diagnosis of acute myocarditis which was confirmed by endomyocardial biopsy in 3; 2) a subendocardial pattern in the mid-apical antero-septal LV segments consistent with myocardial ischemia in one patient with a left anterior descending artery stenosis that was judged as moderate at coronary angiography; 3) a transmural pattern affecting circumferentially the mid-apical LV segments in one patient who received a diagnosis of Tako-tsubo cardiomyopathy.

Left ventricular LGE was present in 18 (69%) patients, including 2 with ischemic distribution (subendocardial or transmural) and 16 with a non-ischemic pattern (midmyocardial or subepicardial). Non-ischemic myocardial fibrosis was found in isolation in 2 patients, and associated with other cardiac diseases in the remaining 15 cases (i.e., cardiomyopathies, N=7; acute myocarditis, N=4; and mitral valve prolapse, N=3).

Right ventricular LGE was present in two patients who fulfilled the International Task Force diagnostic criteria for arrhythmogenic cardiomyopathy[10].

Incremental diagnostic value of CMR

In all 18 patients with obstructive CAD, tissue characterization by CMR confirmed the clinical diagnosis of arrhythmic OHCA due to either acute coronary syndrome (N=12) or chronic ischemic cardiac disease (post-infarction left ventricular scar with no evidence of acute myocardial edema) (N=6).

Among the 26 OHCA survivors with no obstructive CAD, CMR modified the initial clinical diagnosis in 11 (42%). Details are reported in Table 3 and Supplemental file.

Clinical management

An ICD was implanted in all patients with no evidence of acute ischemic injury (no LV myocardial edema), but one who underwent surgical coronary revascularization and had a negative electrophysiological study with programmed ventricular stimulation performed 12 days after surgery. In addition, 5/12 OHCA survivors with evidence of acute myocardial infarction also received an ICD because of severe reduction of LV ejection fraction after 40 days despite optimal medical therapy (N=4) or moderate LV dysfunction in association with non-sustained VT and inducibility of sustained VT at programmed ventricular stimulation (N=1).

Among the 26 OHCA survivors with no obstructive CAD, an ICD was implanted in 22. The remaining 4 OCHA survivors did not receive an ICD for the following reasons: one with mitral valve prolapse and severe mitral regurgitation underwent mitral valve repair and had a negative electrophysiological study with programmed ventricular stimulation 15 days after surgery; one patient with arrhythmogenic cardiomyopathy refused the device implantation; and in 2 patients with acute myocarditis the ICD was deemed not indicated.

Follow-up

Overall, the mean follow-up period was 36±17 months and no patients were lost to follow-up. Five patients experienced appropriate ICD interventions and one patient, who refused ICD implantation, died suddenly. The 6 patients with arrhythmic events during follow-up showed no myocardial edema at CMR while all 18 patients who received a diagnosis of reversible myocardial damage based on CMR evidence of acute myocardial ischemia (N=13), acute myocarditis (N=4) or Tako-Tsubo cardiomyopathy (N=1), had an uneventful arrhythmic outcome. Five patients with obstructive CAD had severe LV dysfunction at CE-CMR: of those, 3 died for non-arrhythmic causes (refractory heart failure, acute myocardial infarction and abdominal aorta aneurysm rupture) and 1 experienced appropriate ICD intervention. The other 5 patients with arrhythmic events during follow-up had a normal or mildly reduced LV function.

DISCUSSION

In survivors of OHCA the identification of the underlying arrhythmic myocardial substrate has important implications for patients' management. Arrhythmic cardiac arrest may be the result of different mechanisms and substrates which include: i) acute and transient electrical instability such that occurring in the setting of acute myocardial ischemia or myocarditis, ii) rapid VT related to a chronic myocardial scar resulting from a previous myocardial infarction or in the context of a cardiomyopathy and iii) primarily electrical disease including genetically-determined ion channel disease, drug toxicity or electrolyte imbalance in the absence of structural heart diseases. With regard to the pathophysiological meaning of myocardial edema, it may either represent the bystander hallmark of an acute cardiac injury (e.g. in acute myocardial infarction) or directly cause ventricular arrhythmias by causing depolarization/repolarization inhomogeneity of myocardium [11].

According to current guidelines[1-2], ICD therapy for secondary prevention of sudden death is reserved to patients with a stable myocardial substrate which exposes to persistent risk of VT/VF relapses. On the contrary, ICD implantation is not justified in patients who suffered VT/VF due to reversible causes, Interpretation of standard investigations such as ECG, echocardiography and coronary angiography may not be straightforward to detect the cause of OHCA and structural substrates of life-threatening ventricular arrhythmias may remain concealed[12-13]; in addition, features of the so-called "post-resuscitation syndrome" may further confuse the clinical diagnosis[3-5].

This study was designed to evaluate the diagnostic yield and prognostic implication of early CMR study with a comprehensive protocol for tissue characterization, including T2-weighted sequences for myocardial edema and post-gadolinium sequences for myocardial fibrosis in a cohort of OHCA survivors with and without obstructive coronary artery disease at coronary angiography who underwent CE-CMR within one week after the event. The main findings were the following: 1)

acute CMR study provided additional value for the identification of causes and mechanisms responsible for arrhythmic OHCA; 2) the evaluation of the presence and regional distribution of both myocardial edema and fibrosis allowed to differentiate acute and reversible myocardial lesions from chronic and stable myocardial substrates, with significant implications on ICD therapy decision-making; 3) identification of acute myocardial edema by CMR predicted an uneventful arrhythmic outcome during follow-up; 4) in our population of OHCA survivors, we did not find any tissue abnormalities at CMR suggestive of post-resuscitation myocardial contusion.

Previous studies

Previous studies showed that CMR provides incremental diagnostic value in patients who survived an OHCA [14-17], but CMR scan protocols were often not uniform and performed late after the acute event, thus reducing the sensitivity of T2-weighted sequences for myocardial edema. Moreover, follow-up data to assess the prognostic value of comprehensive CMR tissue characterization in OHCA are lacking. More details are reported in the supplemental file.

Our results confirm and extend previous observations on the diagnostic and prognostic value of CMR in the setting of OHCA. In our study, the tissue characterization imaging protocol incorporated systematic evaluation of both myocardial edema and LGE in order to distinguish acute and potentially reversible myocardial injury from chronic and irreversible tissue damage[6-7]. At variance with previous studies, all our patients underwent early CMR, i.e. within 7 days of hospitalization, in order to provide the highest sensitivity for detection of transient myocardial edema and were followed-up for a mean of 3 years to prospectively assess the prognostic value of CMR findings.

Diagnostic yield

In patients with obstructive CAD, CMR confirmed the diagnosis of ischemic heart disease by showing LGE with an ischemic distribution (subendocardial or transmural) in all cases. In addition,

T2-weighted sequences allowed to differentiate the arrhythmic substrate due to acute myocardial ischemia, as suggested by the presence of myocardial edema in the territory tributary of a coronary artery, from that of post-infarction myocardial scar[18]. The tissue characterization was also useful for identification or confirmation of the culprit coronary artery, particularly in patients with multiple vessels disease and equivocal coronary angiography findings.

In patients without obstructive CAD, CMR confirmed the clinical diagnosis in 58% of cases and modified the clinical diagnosis in 42% by demonstrating previously unrecognized myocardial substrates. Myocardial edema at T2-weighted sequences was present in 6 cases suggesting that the OHCA was the result of an acute myocardial injury occurring in the setting of acute coronary syndrome, myocarditis or Tako-tsubo cardiomyopathy. In the remaining patients without myocardial edema, ventricular fibrillation was related to cardiomyopathies or recently identified substrates of SCD such as the isolated non-ischemic myocardial scar [13] or the "arrhythmic" mitral valve prolapse (i.e. floppy mitral valve associated with myocardial fibrosis that is localized at the base of the papillary muscle or at the basal posterior wall behind the mitral leaflet) [19].

Prognostic implications

Although definite conclusions cannot be drawn because of the limited sample size, our study results suggest that CMR may provide not only diagnostic but also prognostic information. Compared with tissue characterization based on LGE alone, demonstration of myocardial edema by T2-weighted CMR sequences was of additional value for establishing the acute and potentially reversible nature of the arrhythmic myocardial substrate. These results have the potential to impact ICD decision making because indications to device implantation depends on demonstration of chronic/non-reversible myocardial lesion as the substrate underlying VT/VF[1-2]. In our study, patients with myocardial edema suggesting an acute and potentially reversible myocardial lesion showed no arrhythmic events over a mean follow-up of 3 years. By comparison, 23% of patients without

myocardial edema at CMR, who most likely had a chronic and non-reversible substrate, suffered arrhythmic events during follow-up.

Myocardial damage secondary to resuscitation

The diagnostic accuracy of CMR has been definitely demonstrated in non-OHCA patients and it is now applied in a variety of cardiac conditions. However, clinical interpretation of tissue abnormalities in survivors of OHCA poses additional challenges because all patients received cardiopulmonary resuscitation that may cause cardiac contusion. In our study we found no signs suggestive of post-resuscitation myocardial contusions. Accordingly, myocardial edema at T2-weighted sequences in patients with OHCA should be interpreted as the sign of an underlying disease rather than a non-specific post-resuscitation injury. More details are reported in the Supplemental File.

Study limitations

The main limitations of the study are that it was retrospective and conducted at a single center. Moreover, our study reported on a relatively small number of patients and outcomes because survivors of OHCA were rare and only a minority of them (32%) were eligible for early CMR. Accordingly, our findings should be confirmed by further studies on larger populations and longer follow-up before the use of early CMR for ICD-decision making in survivors of OHCA can be clinically implemented.

In our study, the majority of patients were diagnosed with non-ischemic heart disease in contrast with previous studies demonstrating that obstructive coronary artery disease is the most common cause of OHCA [3]. This finding reflects the selection of patients because only OHCA survivors who were able to undergo early CMR were included in the study. Therefore, the

distribution of OHCA substrates of our study sample cannot be considered representative of the general population.

Conclusions

In survivors of OHCA, tissue characterization by early CMR was of significant diagnostic and prognostic value in addition to standard clinical investigation (Supplemental figures 1 and 2). Demonstration of myocardial edema by T2-weighted sequences, suggesting an acute and potentially reversible myocardial injury, was associated with an uneventful arrhythmic follow-up. These findings suggest that early CMR with T2-weighted sequences may be helpful to guide the decision to implant an ICD for secondary prevention in survivors of OHCA that, according to current guidelines, depends on the exclusion of possible transient and reversible causes for VT/VF such as acute myocardial ischemia or acute myocarditis.

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FIGURES LEGEND

Figure 1. Out-of-hospital cardiac arrest in a patient with obstructive coronary artery disease.
Out-of-hospital cardiac arrest occurring in a 64-year-old male with acute coronary syndrome. Coronary angiography showing multiple vessels obstructive (≥70%) coronary artery stenosis (arrows) affecting both the right (A) and the left (B) coronary artery. Cardiac magnetic resonance showing transmural myocardial edema (three chambers, long axis view; T2-weighted sequences) (C) and subendocardial late gadolinium enhancement (three chamber, long axis view; T1-weighted inversion recovery post-contrast sequences) (D) affecting the infero-lateral left ventricular wall which is tributary of the left circumflex coronary artery.

Figure 2. Out-of-hospital cardiac arrest in a patient with obstructive coronary artery disease.
Out-of-hospital cardiac arrest occurring in a 57-year-old male with post-myocardial infarction scar. Coronary angiography showing multiple vessels obstructive (≥70%) coronary artery stenosis (arrows) affecting both the right (A) and the left (B) coronary artery. Cardiac magnetic resonance showing no myocardial edema (three chambers, long axis view; T2-weighted sequences) (C) and transmural late gadolinium enhancement (three chambers, long axis view; T1-weighted inversion recovery post-contrast sequences) (D) affecting the entire left ventricular lateral wall which is tributary of the left circumflex coronary artery.

Figure 3. Out-of-hospital cardiac arrest in a patient with no obstructive coronary artery disease.
Out-of-hospital cardiac arrest occurring in a 41-year-old male with biopsy-proven acute myocarditis. Coronary angiography showing normal right (A) and left (B) coronary artery. Cardiac

magnetic resonance showing myocardial edema (two chambers, long axis view; T2-weighted sequences) (C) and transmural late gadolinium enhancement (two chambers, long axis view; T1-weighted inversion recovery post-contrast sequences) (D) affecting the mid-apical inferior left ventricular wall.

Figure 4. Out-of-hospital cardiac arrest in a patient with no obstructive coronary artery disease.

Out-of-hospital cardiac arrest occurring in a 29-year-old female with arrhythmic mitral valve prolapse. Coronary angiography showing normal right (A) and left (B) coronary artery. Cardiac magnetic resonance showing thickening and prolapse of both mitral valve leaflets (C,D), no myocardial edema (three chambers, long axis view; T2-weighted sequences) (C) and evidence of mid-myocardial late gadolinium enhancement (three chambers, long axis view; T1-weighted inversion recovery post-contrast sequences) (D) affecting the basal infero-lateral left ventricular wall behind the prolapsing posterior mitral valve leaflet.

Figure 5. Out-of-hospital cardiac arrest in a patient with no obstructive coronary artery disease.

Out-of-hospital cardiac arrest occurring in a 36-year-old male with an isolated non-ischemic left ventricular scar. Coronary angiography showing normal right (A) and left (B) coronary artery. Cardiac magnetic resonance showing no myocardial edema (four chambers, long axis view; T2-weighted sequences) (C) and the presence of subepicardial late gadolinium enhancement (four chambers, long axis view; T1-weighted inversion recovery post-contrast sequences) (D) affecting almost the entire left ventricular lateral wall.

TABLES

Table 1: clinical characteristics of the study population

	Coronary stenosis ≥ 70% N=18	**NO Coronary stenosis ≥ 70% N=26**	**P**
Gender (male)	17 (94%)	19 (73%)	0.11
Age (years)	57 (54-71)	44 (27-59)	<0.001
Risk factors			
Hypertension	13 (72%)	5 (19%)	0.001
Diabetes	6 (33%)	2 (8%)	0.05
Smoking	8 (45%)	4 (15%)	0.04
Dyslipidemia	8 (44%)	5 (19%)	0.09
Family history for CAD	4 (22%)	4 (15%)	0.70
Personal history			
Ischemic heart disease	4 (22%)	0	0.03
Non-ischemic heart disease	0	3 (12%)	0.25
Chest pain within 1 month	6 (33%)	1 (4%)	0.02
Syncope/pre-syncope	0	3 (12%)	0.25
Characteristics of cardiac arrest			
Cardiac arrest in public place	11 (61%)	9 (35%)	0.06
Witnessed cardiac arrest	17 (95%)	23 (88%)	0.63
Bystander CPR	11 (61%)	22 (85%)	0.09
ST-segment elevation post resuscitation	7 (39%)	0	<0.001
Echocardiography at admission			
LV EF (%)	42 (33-50)	50 (47-56)	0.014
LV EDVi (ml/m^2)	71 (56-96)	69 (60-84)	0.40
LV regional WMA	17 (94%)	8 (31%)	<0.001
RV dilation	2 (11%)	5 (19%)	0.68
RV dysfunction	2 (11%)	2 (8%)	0.68
RV regional WMA	1 (6%)	3 (12%)	1.0
Mitral valve regurgitation ≥ moderate	2 (11%)	3 (12%)	1.0
Mitral valve prolapse	0	5 (19%)	0.06
Aortic valve stenosis ≥ moderate	0	0	-
Troponin I peak (umol/L)	5.1 (1.5-82)	1.2 (0.29-9.9)	0.02
Coronary angiography			
At admission	12 (67%)	8 (31%)	0.41
Time from admission	1 (0-3)	2 (1-3)	0.55
Single vessel disease	5 (28%)	0	
Multiple vessel disease with culprit lesion	5 (28%)	0	
Clinical diagnosis (no CMR)			
Structurally normal heart*	0	12 (46%)	<0.001
Ischemic heart disease	18 (100%)	1 (4%)	
Acute myocarditis	0	3 (12%)	
Cardiomyopathy#	0	5 (19%)	
Mitral valve prolapse	0	5 (19%)	

* including Brugada syndrome, idiopathic catecholaminergic ventricular tachycardia, long QT syndrome, and short QT syndrome # including non-ischemic dilated cardiomyopathy, arrhythmogenic cardiomyopathy and hypertrophic cardiomyopathy

CMR=cardiac magnetic resonance; ICD=implantable cardioverter defibrillator; LV=left ventricular; RV=right ventricular; TAPSE=tricuspid annular plane systolic excursion; WMA= wall motion abnormalities; TTS=Tako-tsubo syndrome

Table 2: cardiac magnetic resonance findings in the study population

	Coronary stenosis ≥ 70% N=18	**NO Coronary stenosis ≥ 70% N=26**	**P**
Morpho-functional parameters			
LV systolic function			
Normal	3 (17%)	18 (69%)	<0.001
Mild impairment	3 (17%)	6 (24%)	
Moderate impairment	7 (39%)	2 (8%)	
Severe impairment	5 (28%)	0	
LVEDV			
Normal	7 (39%)	20 (77%)	0.03
Mild dilation	6 (33%)	3 (12%)	
Moderate dilation	2 (11%)	2 (8%)	
Severe dilation	3 (17%)	1 (4%)	
LV regional WMA	17 (94%)	5 (19%)	<0.001
RV systolic impairment	1 (6%)	4 (15%)	0.52
RV dilatation	0	1 (4%)	1.0
RV regional WMA	2 (11%)	3 (12%)	1.0
LV Myocardial edema			
Absent	6 (33%)	20 (77%)	0.002
Patchy, midmyocardial or subepicardial	0	4 (15%)	
Subendocardial	1 (6%)	1 (4%)	
Transmural	11 (61%)	1 (4%)	
LV LGE			
Absent	0	7 (27%)	<0.001
Midmyocardial or subepicardial	0	17 (65%)	
Subendocardial	7 (39%)	1 (4%)	
Transmural	11 (61%)	1 (4%)	
RV LGE	1 (6%)	2 (8%)	1.0
CMR diagnosis			
Structurally normal heart*	0	7 (27%)	<0.001
Ischemic heart disease	18 (100%)	2 (8%)	
Acute myocarditis	0	4 (15%)	
Cardiomyopathy#	0	7 (27%)	
Mitral valve prolapse with LGE	0	3 (12%)	
Tako-Tsubo syndrome	0	1 (4%)	
Non-ischemic LV scar	0	2 (8%)	

CMR=cardiac magnetic resonance; LGE=late-gadolinium enhancement; LVEDV= left ventricular end-diastolic volume; LV=left ventricular; RV=right ventricular; WMA= wall motion abnormalities;

including non-ischemic dilated cardiomyopathy, arrhythmogenic cardiomyopathy and hypertrophic cardiomyopathy

435 **Table 3** – comparison between clinical and cardiac magnetic resonance diagnosis

Suspected diagnosis (pre-CMR)	**Final diagnosis (after-CMR)**	**Agreement**
Structurally normal heart (N=12)	Structurally normal heart = 7	7/12 (58%)
	Acute myocarditis = 2	
	Cardiomyopathy = 1	
	Non-ischemic LV scar = 2	
Ischemic heart disease (N=19)	Ischemic heart disease = 18	18/19 (95%)
	Tako-tsubo syndrome = 1	
Acute myocarditis (N=3)	Acute myocarditis = 1	1/3 (33%)
	Ischemic heart disease = 1	
	Cardiomyopathy = 1	
Cardiomyopathy (N=5)	Cardiomyopathy = 4	4/5 (80%)
	Ischemic heart disease = 1	
Mitral valve prolapse (N=5)	Mitral valve prolapse with LGE = 3	3/5 (60%)
	Cardiomyopathy = 1	
	Acute myocarditis = 1	
Agreement	**Coronary stenosis ≥70% group**	18/18 (100%)
	NO coronary stenosis ≥70% group	15/26 (58%)
	Overall agreement	33/44 (75%)

436 CMR=cardiac magnetic resonance; LGE=late gadolinium enhancement; LV=left ventricular